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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/019,441	02/05/98	REFF M	012712-502

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EXAMINER	
DIBRINO, M	
ART UNIT	PAPER NUMBER
1644	25

DATE MAILED: 04/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/019,441	Reff et al.
Examiner	**Group Art Unit**
Mariann DiBrino	1644

☒ Responsive to communication(s) filed on *Feb 7, 2001*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1, 2, and 4-39* is/are pending in the applicat

Of the above, claim(s) *26-39* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 2, and 4-25* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's amendment, filed 2/7/01 (Paper No. 22), is acknowledged and has been entered.

Claims 1, 2, and 4-25 are being acted upon presently.

Applicant's amendment to delete the sequence on page 57 at line 24 is acknowledged.

2. Applicant's terminal disclaimer filed 2/7/01 over U.S. Patent No. 6,011,138 is acknowledged and is acceptable.

In view of Applicant's amendment filed 2/7/01 only the following rejections remain.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

4. Claims 1, 2, 4-9 and 14-22 stand rejected under 35 U.S.C. 102(a) as being anticipated by Bonnefoy et al (WO 96/12741) as evidenced by Saxon et al (J. Immunol. Vol. 147 (11), 1991, pp 4000-4006) for the reasons of record in the Office Action mailed 4/25/00 (Paper No. 13).

Applicant's arguments in the amendment filed 4/7/01 have been fully considered but are not persuasive.

It is Applicant's position at page 2 of the said amendment that Bonnefoy et al fails to teach any particular anti-CD23 antibody meeting the claim limitations and the said reference does not exemplify the said antibody.

It is the Examiner's position that the reference teaches anti-CD23 monoclonal antibodies that have a human IgG1 or IgG3 constant region, whether or not the antibodies were actually reported made, and that Saxon et al evidence that it is an inherent property of anti-CD23 antibodies to inhibit IgE expression.

It is the Applicant's further position that the Bonnefoy et al reference could be applied as a 103(a) type reference, and Applicant argues potential obviousness issues. It is Applicant's position at the last paragraph of page 3 of the said amendment, and continuing onto page 4, first two paragraphs, that while Saxon et al demonstrate that anti-CD23 antibodies can inhibit IgE expression, it could not have been reasonably predicted that such inhibiting activity would

correlate to the presence or absence of particular human constant domains. Applicant further argues that Flores Romo et al (Science, 261: 1038-1041, 1993), not provided to the Examiner, reported Fabs that were capable of inhibiting IgE antigen-specific responses comparably to intact antibodies, and that hence, there would have been no reason to produce a chimeric antibody as claimed because the reasonable expectation would have been that it would not affect the desired function (IgE inhibition) and potentially would unnecessarily increase costs associated with antibody manufacture.

It is the Examiner's further position that Bonnefoy et al teach anti-CD23 antibodies in pharmaceutical compositions, and that the human constant domains of such antibodies elicit a negligible immune response when administered to a human compared to the immune response mounted by a human against a rat or mouse antibody (page 5 at lines 4-11, these lines cited in the last Office Action), a substantial reason to produce such a chimeric antibody. It is not necessary that the inhibiting activity of anti-CD23 antibodies be correlated to the presence or absence of particular human constant domains. In addition, in the Flores Romo et al reference cited by Applicant, Applicant argues that the Fabs taught by Flores Romo et al were capable of inhibiting IgE antigen-specific responses; however, inhibition of IgE antigen-specific responses is not necessarily inhibition of IgE expression.

It is the Applicant's position that the inventors have surprisingly discovered that the presence of human constant domains is highly significant to IgE inhibition based on a comparison of two primate antibodies, and Applicant points to pages 17-18 of the specification. In the specification, it is Applicant's position that antibodies with a $\gamma 1$ constant region is superior to the primate antibodies or to chimeric antibodies with an $\gamma 4$ human constant region in the inhibition of IL-4 induced IgE expression.

It is the Examiner's position that these two primate antibodies disclosed and discussed on pages 17-18 of the instant specification are 5E8 and 6G5, and data for these antibodies and their primatized, i.e., chimeric human constant region, $\gamma 1$ and $\gamma 4$ containing, counterparts are disclosed in Figures 3 and 5 and in the Brief Description of the Drawings for the said figures. In the instance of the 6G5 series of antibodies shown in Figure 5, the primate antibody (6G5) , and the primatized antibodies with either the $\gamma 1$ (6G5G1) or $\gamma 4$ (6G5G4) human constant regions perform the same at all three concentrations of antibody in the inhibition of production of IL-4 induced IgE expression, noting the standard error bars. In the instance of the 5E8 series of antibodies shown in Figure 3, the primatized antibodies with the $\gamma 1$ human constant region (5E8G1 and 5E8G1N) perform comparably to the primatized antibodies with the $\gamma 4$ human constant region (5E8G4P and 5E8G4PN) at the lowest concentrations of antibody and one (5E8G4P) performs perhaps slightly better at the highest concentration of antibody, noting the standard error bars.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 2, 4-11 and 14-24 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Queen et al (U.S. Patent No. 5,585,089) in view of Saxon et al (J. Immunol. Vol. 147 (11), 1991, pp 4000-4006) for the reasons of record in the Office Action mailed 4/25/00 (Paper No. 13).

Applicant's arguments in the amendment filed 4/7/01 have been fully considered but are not persuasive.

It is the Applicant's position on page 4 of the said amendment at the first full paragraph, that neither reference renders the subject monoclonal antibodies obvious given the unexpected discovery made by the inventors, i.e., that the presence of particular human constant domains significantly enhances IgE inhibiting activity.

It is the Examiner's position that the Examiner's comments in item #4 of this Action at the last two paragraphs applies to the Applicant's arguments as to the issue of unexpected results.

It is the Applicant's position on page 4 of the said amendment at the second full paragraph, that the instant rejection should be withdrawn because "it is directly inconsistent with the issuance of U.S. Patent 6,011,138. It is the Applicant's further position that "However, based on substantially the same arguments as set forth herein, the Examiner vacated such rejection as she agreed that the effect of the human constant domains on IgE inhibiting activity are truly unexpected and not suggested by Queen et al or Saxon et al."

As to Applicant's statement supra about U.S. Patent 6,011,138, the Examiner does not know what is meant by "directly inconsistent with the issuance of U.S. Patent 6,011,138". With regard to the rest of Applicant's argument, the Examiner did not vacate the said rejection because she agreed that the effect of the human constant domains on IgE inhibiting activity are truly unexpected and not suggested by Queen et al or Saxon et al. The said rejection was

vacated on the basis of the primary reference Wakai et al.

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1, 2 and 4-25 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of copending Application No. 09/292,053. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the'053 application, i.e., an anti-human CD23 monoclonal antibody comprising a human gamma-1 constant region, is encompassed by the claims of the instant application. Although the 5E8, 6G5 or 2C8 antibodies recited in the '053 application are not recited in the instant claims, SEQ ID NOS: 1-4 which are recited in the instant claims are derived from said antibodies.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's request in Applicant's amendment filed 2/7/01 to hold this rejection in abeyance is noted. However, until a terminal disclaimer is filed, the rejection stands.

The following are new grounds of rejection necessitated by Applicant's amendment filed 2/7/01.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 16 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 is indefinite for depending upon canceled claim 3. Applicant is required to rewrite claim 16 in independent form.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 2, 5-9, 14, 15 and 17-22 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Newman et al (U.S. Patent No. 5,658, 570, of record) in view of Saxon et al (J. Immunol. Vol. 147 (11), 1991, pp 4000-4006, of record).

Newman et al disclose human, chimeric or humanized anti-CD23 antibodies which comprise a human constant region of IgG isotype (especially claims 1-8 and column 8, lines 52-53 and lines 24-29) and which comprise a primate antigen binding portion, and pharmaceutical compositions thereof (especially column 2 and column 26, lines 8-20). Newman et al disclose an anti-CD4 monoclonal antibody with a human gamma 1 isotype constant region (especially column 18 at lines 51-53 and claims 33-35).

Newman et al do not disclose a chimeric or humanized anti-CD23 antibody with a human gamma 1 isotype constant region, and Newman et al do not teach that anti-CD23 antibodies inhibit IgE expression.

Saxon et al teach that anti-CD23 antibodies inhibit IgE expression (especially Abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the gamma 1 isotype constant region of the anti-CD4 antibody disclosed by Newman et al as the IgG isotype in the anti-CD23 antibodies also disclosed by Newman et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because the gamma 1 is an isotype of IgG and was used by Newman et al in another chimeric monoclonal antibody.

Claims 8 and 21 are included in this rejection because the ability to inhibit IgE expression in vivo is an expected property of said antibodies because they have this property in vitro. It is an expected property of said antibodies to bind to the human Fc gamma receptors.

Applicant's arguments in the amendment filed 4/7/01 have been fully considered but are not persuasive.

It is Applicant's position on page 3 beginning at the second full paragraph in the said amendment that the Newman et al reference does not render obvious the claimed antibodies or pharmaceutical compositions thereof, and that the rejection should be withdrawn on the basis of unexpected results. It is the Applicant's further position that it could not have been reasonably predicted, nor was it obvious, that a human gamma 1 or gamma 3 anti-human CD23 monoclonal antibody would inhibit IgE production better than an otherwise equivalent anti-human CD23.

It is the Examiner's position that the Examiner's comments in item #4 of this Action at the last two paragraphs applies to the Applicant's arguments as to the issue of unexpected results. It is the Examiner's further position that it is not necessary that it be reasonably predicted, nor obvious, that a human gamma 1 or gamma 3 anti-human CD23 monoclonal antibody would inhibit IgE production better than an otherwise equivalent anti-human CD23 because would have been sufficient motivation to have used a human gamma 1 constant region for the reasons enunciated supra in the instant rejection.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne DiBrino whose telephone number is (703) 308-0061. The examiner can normally be reached Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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Group 1640
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April 10, 2001

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